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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/693,301 | 10/24/2003 | Gary K. Schwartz | 702-A-US | 1477 |

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| EXAMINER | |
|---|---|
| MARTIN, PAUL C | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1657 | |

| MAIL DATE | DELIVERY MODE |
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| 11/21/2007 | PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/693,301 | SCHWARTZ, GARY K. | |
| | Examiner | Art Unit | |
| | Paul C. Martin | 1657 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *10 September 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *34-38,41 and 42* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *34-38,41 and 42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *06 February 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *09/10/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

Claims 34-38, 41 and 42 are pending in this application and were examined on their merits.

### *Continued Examination Under 37 CFR 1.114*

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 09/10/07 has been entered.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 36 and 37 are newly rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 36 requires the sequential administration of the coptis chinesis extract and the therapeutic agent, while claim 37 requires that that subject be treated with the coptis chinesis extract first and then the therapeutic agent. As Claim 36 is dependent upon Claim 34 which requires administering a composition comprising aqueous coptis chinesis extract, a therapeutic agent and a protein kinase C inhibitor it is unclear how: a) one will sequentially administer individual components out of a composition and b) what happens to the protein kinase C inhibitor in dependent Claims 36 and 37.

Claims 38 and 42 are newly rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 38 requires administering a composition comprising aqueous coptis chinesis extract and a microtubule destabilizing agent wherein the subject is treated with the aqueous coptis chinesis extract first and then with the microtubule destabilizing agent. It is unclear how one will sequentially administer individual components out of a composition. Claim 42 is rejected as being dependent upon rejected Claim 38.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 34-38, 41 and 42 are rejected under 35 U.S.C. 103(a) as being obvious over Li *et al.* (2000).

Li *et al.* teaches a method for inhibiting the cell growth in human (gastric, colon and breast) cancer cells by administering an effective amount or aqueous coptis chinesis (huanglian) extract (Pg. 1287, Column 2, Lines 10-19 and Pg. 1288, Column 1, Lines 1-7 and Pg. 1289, Fig. 1).

Li *et al.* teaches the administration of the known anti-tumorigenic microtubule-destabilizing compound nocodazole followed by coptis chinesis extract, 54% of human gastric cancer cells accumulated in the $G_2$ phase (cell cycle block antimitotic) and that huanglian suppressed cyclin B1 protein expression by 70% and inhibited cdc2 kinase activity by 90% (Pg. 1292, Column 1, Lines 4-20 and Table 1); and that Protein Kinase C inhibitors such as Flavopiridol were known to inhibit tumor cell growth and have entered clinical trials as an anticancer treatment (Pg. 1292, Column 2, Lines 10-19).

Li *et al.* teaches that huanglian is part of a class of novel agents that inhibit tumor growth and suggests the use of huanglian as an oral anticancer drug (Pg. 1293, Column 1, Lines 45, 46 and 54-57).

Li *et al.* teaches that 100% tumor growth inhibition can only be achieved using the whole herbal extract, rather than its individual components, for cancer therapy (Pg. 1293, Column 1, Lines 25-34).

Li *et al.* does not teach the administration of an effective amount of aqueous *coptis chinesis* extract, a therapeutic agent, and a protein kinase C inhibitor or taxol-like nocodazole microtubule-destabilizing compound; or wherein the administration is performed in a sequential manner with *coptis chinesis* extract first then a therapeutic agent or microtubule-destabilizing agent.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to modify the teachings of Li *et al.* to treat cancer in a subject by administering an effective amount of huanglian, the therapeutic agent nocodazole and the protein kinase C inhibitor; treating cancer in a subject by administering an effective amount of huanglian and the microtubule-destabilizing agent nocodazole wherein the subject is treated with huanglian first and then the nocodazole because the combination of three known compounds (in the case of Claim 34) with anti-cancer properties to form one treatment would have been recognized as obvious by one of ordinary skill in the art at the time of the invention.

The MPEP states:

> "It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980).

One of ordinary skill in the art at the time of the invention would have recognized that the *in vitro* data demonstrating the effectiveness of nocodazole and huanglian would lead one of ordinary skill in the art to the recognition that each is cabable of being utilized as a treatment of cancer in a subject *in vivo*.

The MPEP states:

> Similarly, courts have found utility for therapeutic inventions despite the fact that an applicant is at a very early stage in the development of a pharmaceutical product or therapeutic regimen based on a claimed pharmacological or bioactive compound or composition. The Federal Circuit, in *Cross v. Iizuka*, 753 F.2d 1040, 1051, 224 USPQ 739, 747-48 (Fed. Cir. 1985), commented on the significance of data from in vitro testing that showed pharmacological activity:
>
> We perceive no insurmountable difficulty, under appropriate circumstances, in finding that the first link in the screening chain, in vitro testing, may establish a practical utility for the compound in question. Successful in vitro testing will marshal resources and direct the expenditure of effort to further in vivo testing of the most potent compounds, thereby providing an immediate benefit to the public, analogous to the benefit provided by the showing of an in vivo utility.

Finally, one of ordinary skill in the art at the time of the invention would have recognized that the sequential administration of the huanglian extract followed the microtubule-destabilizing agent nocodazole would have been obvious as the sequence of adding ingredients (or treatments) is not considered non-obvious.

The MPEP states:

*Ex parte Rubin* , 128 USPQ 440 (Bd. App. 1959) (Prior art reference disclosing a process of making a laminated sheet wherein a base sheet is first coated with a metallic film and thereafter impregnated with a thermosetting material was held to render prima facie obvious claims directed to a process of making a laminated sheet by reversing the order of the prior art process steps.). See also *In re Burhans*, 154 F.2d 690, 69 USPQ 330 (CCPA 1946) (selection of any order of performing process steps is prima facie obvious in the absence of new or unexpected results); In re Gibson, 39 F.2d 975, 5 USPQ 230 (CCPA 1930) (Selection of any order of mixing ingredients is prima facie obvious.).

No Claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Paul C. Martin whose telephone number is 571-272-3348. The examiner can normally be reached on M-F 8am-4:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Paul Martin
Examiner
Art Unit 1657

11/13/07

/Jon P. Weber/
Jon P. Weber
Supervisory Patent Examiner, 1657